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EXAMINER

OLSON, ERIC

ART UNIT	PAPER NUMBER
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1623

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,484	Applicant(s) CHEUNG, NAI-KONG V.	
	Examiner ERIC S. OLSON	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 January 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>July 24, 2006</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

This application is a national stage application of PCT/US04/23099, filed July 16, 2004, which is a continuation in part of US application 10/621027, filed July 16, 2003, currently allowed, which is a continuation in part of international application PCT/US02/01276, filed January 15, 2002, which claims benefit of provisional application 60/261911, filed January 16, 2001. Claims 1-13 are pending in this application and examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising a beta-glucan and one or more specific monoclonal antibodies for the treatment of specific cancers, does not reasonably provide enablement for compositions comprising any anti-tumor antibody whatsoever for the treatment of any cancer whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a

disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is drawn to compositions comprising an antibody and a glucan which are suitable for the treatment of cancer.

The state of the prior art: The prior art discloses various monoclonal antibody therapies against tumors. The prior art also discloses that beta-glucan produces an anti-tumor effect *in vivo* by stimulating the immune system against a tumor, and can enhance the effects of both endogenous and exogenous antibodies. The current state of the art in antibody therapy is not such that a routine, predictable, and effective antibody therapy exists for each and every cancer which could possibly be encountered.

With regards to generalizing specific results to the treatment of all cancers, the skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. No single therapy is useful for the treatment of every case of cancer. Indeed, some types of cancer do not respond well to any known chemotherapeutic drugs. According to the Merck Manual of Diagnosis and Therapy (Reference included with PTO-892), Hepatocellular carcinomas and renal cell carcinomas are not generally improved by chemotherapy. Acute lymphoblastic

leukemia, on the other hand, responds well to a number of drugs, including vincristine, anthracyclines, and aspariginases, while acute mylogenous leukemia, on the other hand, responds to fewer drugs and is usually treated with cytarabine in combination with daunorubicin or idarubicin. Breast cancer, on the other hand, is best treated with surgery and/or radiation, but the prognosis can be improved by the addition of adjuvant chemotherapy. While results for antibody-based therapies are less completely studied, there is no reason for one skilled in the art to expect that tumors will display less heterogeneity with respect to antibody therapy.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: As mentioned above, no single treatment is effective for all cancers. Different cancers vary widely in their response to different chemotherapy regimens. According to the Oxford Textbook of Oncology, (Reference cited in PTO-892) "The important criteria for the tumor include its sensitivity to cytostatic drugs, its clinical stage and its mass, the presence of measurable lesions or biochemical markers, and, finally, growth characteristics," as well as, "*In vitro* sensitivity tests have been disappointing. They predict well for resistance but are of little use for sensitivity," (p. 451, right column, second paragraph) and, "For many types of cancer the potential benefit of chemotherapy has not been demonstrated in well-designed clinical trials."

Based on the known teachings of the prior art such as that stated above, one skilled in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: gynecological

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tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CAN, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute and chronic leukemias and benign papillomatosis tumors, by performing the necessary experimentation to develop an optimized dose-dense protocol for treating said cancers.

There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. The treatment of cancer is highly unpredictable due to the differing forms of cancerous cells, their location, their potential for metastases, the fact that cancer therapeutics are palliative rather than curative and that cancer treatment readily harms normal tissues. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent

to be effective against cancers or tumor cells generally by enhancing the effectiveness of antibodies generally or the wherein the antibody is capable of activating complement or dependent cell-mediated cytotoxicity

Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Because monoclonal antibodies and other immunological therapies are not as well established and predictable as conventional cytotoxic chemical chemotherapy, they face a higher burden of enablement. Applicant's methods do not involve known drugs for which comprehensive pharmacological data, such as optimal dosages and effectiveness against specific cancers, is not yet available.

The Breadth of the claims: The claimed methods and compositions include antibodies capable of treating any cancer whatsoever, regardless of cause, parent cell type, antigen expression, and therapeutic resistance.

The amount of direction or guidance presented: Applicant's specification discloses that exogenous antibodies can be rendered more effective against cancer by the co-administration of beta-glucan. However, Applicant's specification does not define the limits of this therapy or provide a reasonable basis by which one skilled in the art may conclude that it is generally applicable to all cancers.

The presence or absence of working examples: Working examples are provided for therapies against specific tumors using antibodies against specific targets. These

examples are not sufficient to be representative of every possible tumor which could conceivably afflict a subject.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as synergistic beta-glucan/antibody therapy. See MPEP 2164.

The quantity of experimentation necessary: In order to use the disclosed information to practice the claimed invention for a wide range of cancers using a wide range of antibodies, a skilled practitioner of the art would develop a wide variety of antibodies against a wide variety of targets. This would involve a process of optimizing and testing various regimens *in vivo* for each type of cancer being treated. Because the art is still undeveloped, this process would involve unpredictable experimentation which would constitute an undue experimental burden on the practitioner.

Genentech, 108 F.3d at 1366, states that, “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion.” And “patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

Therefore, in view of the Wands factors, as discussed above, particularly the unpredictability of the art and the lack of guidance and working examples, Applicants fail to provide information sufficient to practice the claimed invention for compositions for the treatment of all possible tumors with all possible tumor-binding antibodies.

Claims 1, 2, 5, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising specific chemotherapeutic agents known in the prior art or disclosed in Applicant's specification, does not reasonably provide enablement for compositions comprising any substance or any chemotherapeutic agent whatsoever. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a pharmaceutical composition. In order for a pharmaceutical composition to be enabled, it must be possible, absent undue experimentation, for one skilled in the art to obtain each component of the composition, for example commercially or by chemical synthesis.

The state of the prior art: A wide variety of chemotherapeutic substances are known in the art. Treatment of cancer using these substances is well known in the art. However, the art does not include a complete knowledge of all possible

chemotherapeutic substances, or a method for determining said scope that does not involve extensive testing of all potential chemotherapeutic agents.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: While certain general classes of chemotherapeutic agents are known (e.g. DNA damaging agents, nucleosides, hormone mimetics) One skilled in the art cannot thereby extrapolate to all possible mechanisms of selectively killing cancer cells or all possible compounds that fulfill said mechanisms. Rather, one skilled in the art could only discover new chemotherapeutic agents by selectively testing a representative sample of potential lead compounds.\

Furthermore, the synthesis of novel chemical compounds is unpredictable as well. The development of a novel synthetic pathway will involve an unpredictable process of trial and error in order to find a synthetic method that is acceptable. While certain general synthetic strategies can be extrapolated from known synthetic methods, actually putting the synthesis into practice will involve highly unpredictable experimentation.

The Breadth of the claims: The claimed invention is very broad, including compositions comprising all possible chemotherapeutic agents. This is interpreted as all chemical substances safe for *in vivo* use that are capable of killing, arresting, or reducing a tumor.

The amount of direction or guidance presented: Applicant's specification describes beta-glucans and monoclonal complement-activating antibodies, which could

reasonably be considered to be chemotherapeutic agents as they are effective in killing cancer cells. However, the specification does not disclose the full range of all possible chemotherapeutic agents or provide any means of determining the limits of said range save for repeatedly obtaining and assaying a representative sample of all possible chemotherapeutic agents.

The presence or absence of working examples: The only working examples provided concern the immunological treatment of cancer by co-administering beta glucans and complement activating monoclonal antibodies.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the discovery of broad classes of novel compounds. See MPEP 2164.

The quantity of experimentation necessary: One of ordinary skill in the art, in order to practice the claimed invention with the full range of chemotherapeutic agents beyond the meager number disclosed in the specification would be required to test potential compounds *in vivo* to determine whether a particular compound is useful as a chemotherapeutic agent. According to the 2006 Chemical Abstracts catalog, (Reference included with PTO-892) The Chemical Abstracts Registry contains entries for approximately 26 million compounds, all of which are potentially included in the claimed invention if they happen to have anti-cancer activity. For most compounds, it is unknown whether they are or are not useful as chemotherapeutic agents. Gathering this data for every compound known to man would involve *in vitro* screening of an enormous diversity of chemical compounds for anti-tumor activity, as well as *in vivo*

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testing of compounds having this activity involving either human or animal subjects to determine therapeutic utility. *In vitro* testing requires that the compounds to be tested be synthesized and subjected to an appropriate screening method. As described earlier, synthesis of diverse chemical structures requires novel and unpredictable experimentation in order to develop suitable synthetic methods. *In vivo* animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Human tests impose even greater ethical and regulatory burdens, as well as additional difficulty locating subjects. Because of the unpredictability of the art and the lack of comprehensive working examples covering any significant portion of the total number of potential chemotherapeutic agents, these animal experiments would need to be repeated hundreds of times, and involve the maintenance, killing, dissection, and disposal of thousands of experimental animals, to establish the activity or lack thereof of every possible chemotherapeutic agent, thus presenting an a burden of undue experimentation to anyone practicing the invention with the full range of chemotherapeutic agents claimed.

Genentech, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the lack of guidance or working examples, Applicants fail to provide information sufficient to practice the claimed invention for compositions comprising all possible chemotherapeutic agents.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yan et al. (Citation no. 78 in PTO-1449).

Yan et al. discloses a yeast-derived beta-glucan composition (denoted as SZP_g) capable of producing a synergistic complement-mediated antitumor effect in a mouse xenograft model of breast cancer (p. 304, right column) in combination with antitumor antibodies. (p. 3048, left column and figure 3) The beta-glucan has a 1,3-linked backbone and is branched with 1,6-linked side chains, (p. 3045, left column, first paragraph) and is obtained from yeast. (zymosan) It has a molecular weight of about 10000 kDa. (p. 3046, left column, last paragraph) On p. 11, lines 9-12 of the instant

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specification, "high molecular weight" is defines as being at least 10000 **daltons**.

Therefore the SZP of Yan et al. is high molecular weight as described in the instant claims. The combination therapy led to a synergistic effect producing more than additive results in the mice. It is explained that the normal antitumor effect of beta-glucans is only present in specific strains of mice having appropriate antibodies toward the tumor, and that the addition of exogenous antitumor antibodies can restore this activity in cases in which beta-glucan monotherapy is ineffective. (p. 3050, under the heading **Discussion**) Anti-GD2 antibodies are cited as a specific example. (p. 3050, right column, first paragraph) Note that the claimed composition is described in the base claim 1 as a composition "comprising an appropriate amount of carbohydrates." While dependent claims such as 5, 8, and 11-13 define the substance that can be enhanced by the beta-glucan, these claims are worded in such a way that they do not actually require the substance to be present in the composition, so long as the composition could theoretically enhance said substance if they were co-administered. Therefore the zymosan polysaccharide described by Yan et al. is identical to the carbohydrate described in the instant claims. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Thus Yan et al. anticipates the claimed invention.

However, assuming for the sake of argument that the instant claims are interpreted to require a composition comprising both the carbohydrate and the additional substance, claims 1-13 are rejected under 35 USC 103(a) for being obvious over Yan et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a pharmaceutical composition comprising both a beta-glucan and one of the antibodies of Yan et al. One of ordinary skill in the art would have been motivated to produce a pharmaceutical composition comprising a beta-glucan and an antibody because the method of Yan et al. comprises concurrently administering both of these active ingredients to a subject. One of ordinary skill in the art would reasonably have expected success in combining the ingredients because the prior art explicitly suggests administering them at the same time to the same subject. Combining two prior art active agents known to be useful when co-administered is well within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 1-13 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Herlyn. (US patent 5130127, cited in PTO-1449) Herlyn discloses that co-administration of $\beta(1\rightarrow3)$ glucan lentinan and anti—tumor monoclonal antibodies has the effect of increasing the anti-tumor effect of the antibodies. (column 1 lines 47-67, column 2 lines 25-30) The average molecular

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weight of the lentinan used is between 4×10^5 and 8×10^5 , which is considered to be high molecular weight according to the definition given on p. 11, lines 9-12 of the instant specification. (column 2 lines 38-42) This enhancement occurs through complement activation. (column 3, lines 40-45) Although Herlyn does not say that lentinan has (1-6) side chains, Kidd (reference 59 cited in PTO-1449) discloses that lentinan is a β 1-3, β 1-6 glucan. (p. 6, left column first paragraph) Therefore the lentinan used by Herlyn is reasonably considered to have 1,3-1,6 mixed linkages according to instant claims 4 and 10. Note that the claimed composition is described in the base claim 1 as a composition "comprising an appropriate amount of carbohydrates." While dependent claims such as 5, 8, and 11-13 define the substance that can be enhanced by the beta-glucan, these claims are worded in such a way that they do not actually require the substance to be present in the composition, so long as the composition could theoretically enhance said substance if they were co-administered. Therefore the lentinan polysaccharide described by Herlyn is identical to the carbohydrate described in the instant claims. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Therefore Herlyn anticipates the claimed invention.

However, assuming for the sake of argument that the instant claims are interpreted to require a composition comprising both the carbohydrate and the additional substance, claims 1-13 are rejected under 35 USC 103(a) for being obvious over Herlyn.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a pharmaceutical composition comprising both a beta-glucan lentinan and one of the antibodies of Herlyn. One of ordinary skill in the art would have been motivated to produce a pharmaceutical composition comprising a beta-glucan and an antibody because the method of Herlyn comprises concurrently administering both of these active ingredients to a subject. One of ordinary skill in the art would reasonably have expected success in combining the ingredients because the prior art explicitly suggests administering them at the same time to the same subject. Combining two prior art active agents known to be useful when co-administered is well within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Suzuki et al. (Reference 71 included with PTO-1449) Suzuki et al. discloses that lentinan exerts synergistic antitumor effects when combined with various therapies such as chemotherapy, (e.g. fluorouracil in table 1) even against tumors resistant to lentinan alone. (p. 464, left column first paragraph, also table 1, p. 465 fig. 1) Kidd (reference 59 cited in PTO-1449)

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discloses that lentinan is a β 1-3, β 1-6 glucan with a molecular weight of about 4000-1000000, which is a high molecular weight according to the definition given on p. 9, lines 9-12 of the instant specification. (p. 6, left column first paragraph of Kidd)

Therefore the lentinan used by Suzuki et al. is reasonably considered to have 1,3-1,6 mixed linkages according to instant claims 4 and 10. Note that the claimed composition is described in the base claim 1 as a composition "comprising an appropriate amount of carbohydrates." While dependent claims such as 5 define the substance that can be enhanced by the beta-glucan, these claims are worded in such a way that they do not actually require the substance to be present in the composition, so long as the composition could theoretically enhance said substance if they were co-administered. Therefore the lentinan polysaccharide described by Suzuki et al. is identical to the carbohydrate described in the instant claims. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Therefore Suzuki et al. anticipates the claimed invention.

However, assuming for the sake of argument that the instant claims are interpreted to require a composition comprising both the carbohydrate and the

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additional substance, claims 1-7 and 9 are rejected under 35 USC 103(a) for being obvious over Suzuki et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a pharmaceutical composition comprising both a beta-glucan lentinan and a chemotherapeutic agent according to Suzuki et al. One of ordinary skill in the art would have been motivated to produce a pharmaceutical composition comprising a beta-glucan and a chemotherapeutic agent because the method of Suzuki et al. comprises concurrently administering both of these active ingredients to a subject. One of ordinary skill in the art would reasonably have expected success in combining the ingredients because the prior art explicitly suggests administering them at the same time to the same subject. Combining two prior art active agents known to be useful when co-administered is well within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 1-7 and 9 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jamas et al. (US patent 5504079, cited in PTO-892) Jamas et al. discloses immunostimulatory yeast glucan preparations containing $\beta(1-6)$ and $\beta(1-3)$ glycosidic linkages. (column 2 lines 38-67) Immunomodulatory glucans having this backbone include alkali-insoluble yeast glucan, lentinan, scleroglucan, and schizophyllan. (column 4, lines 31-51) These glucans can be administered to treat subjects who are at heightened risk of infection due to various circumstances including chemotherapy. (column 6, lines 55-67) Thus they are useful for

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enhancing the efficacy of a chemotherapeutic agent by reducing the side effects produced by said agent. Kidd (reference 59 cited in PTO-1449) discloses that lentinan has a molecular weight of about 4000-1000000, and schizophyllan has a molecular weight of about 450000 daltons, which are high molecular weights according to the definition given on p. 9, lines 9-12 of the instant specification. (p. 6, left column first and second paragraphs of Kidd) Note that the claimed composition is described in the base claim 1 as a composition "comprising an appropriate amount of carbohydrates." While dependent claims such as 5 define the substance that can be enhanced by the beta-glucan, these claims are worded in such a way that they do not actually require the substance to be present in the composition, so long as the composition could theoretically enhance said substance if they were co-administered. Therefore the polysaccharides described by Jamas et al. is identical to the carbohydrate described in the instant claims. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. Therefore Jamas et al. anticipates the claimed invention.

However, assuming for the sake of argument that the instant claims are interpreted to require a composition comprising both the carbohydrate and the

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additional substance, claims 1-7 and 9 are rejected under 35 USC 103(a) for being obvious over Jamas et al.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare a pharmaceutical composition comprising both a beta-glucan and a chemotherapeutic agent according to Jamas et al. One of ordinary skill in the art would have been motivated to produce a pharmaceutical composition comprising a beta-glucan and a chemotherapeutic agent because the method of Jamas et al. comprises concurrently administering both of these active ingredients to a subject. One of ordinary skill in the art would reasonably have expected success in combining the ingredients because the prior art explicitly suggests administering them at the same time to the same subject. Combining two prior art active agents known to be useful when co-administered is well within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 193 of copending Application No. 10/621027. (Cited in PTO-892 as US patent publication 2004/0116379, herein referred to as '027) Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 193 of '027 anticipates the claimed invention. Specifically, this claim is drawn to a composition of a barley (1-3)beta glucan and a complement-activating antibody that binds to a cancer cell, wherein the glucan enhances the antibody's anti-tumor activity. This claim therefore falls within the limitations of all of instant claims 1-13, anticipating the claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. However, '027 has been allowed. Therefore this rejection cannot be held in abeyance.

Claims 1, 3, and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of copending Application No. 11/334763. (Cited in PTO-892 as US patent publication 2006/0160766, herein referred to as '763) Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 11 of '763 anticipates the claimed

invention. In particular, this claim is drawn to an effective amount of beta-glucan effective for deliver of peptide, protein, RNA, DNA, or plasmid, thus reciting the same limitations as the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
2/13/2008

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623